Remarks

Claims 31, 33, 35 and 59-77 were previously pending. Following entry of this amendment, claims 35 and 59-91 will be pending. Claims 72-77 have been withdrawn from consideration. Claims 35, 60, 64, 67 and 70 have been amended. Claims 31 and 33 have been canceled. By the present amendment, claims 35, 60, 64, 67 and 70 have been amended to recite the deposit information. Support for this amendment can be found for example in the paragraph beginning with the phrase "All hybridomas" on page 30, of the specification as filed. Claims 64, 67 and 70 have also been amended to recite that the humanized antibody binds to an ACT-4 receptor polypeptide. Support for this amendment can be found for example on page 33, lines 13-15, of the specification as filed. New claims 78-91 find support on page 33, line 13, to page 38, line 13, of the specification as filed. No new matter is added by these amendments.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 31, 33, 35 and 59-72 have been rejected under 35 U.S.C. § 112, first paragraph, for purportedly containing subject matter not described in the specification in such a way as to enable one of skill in the art to make and/or use the invention. For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

Initially, the Examiner has requested that a Deposit Declaration be filed, indicating that the L106 antibodies have been deposited under the terms of the Budapest treaty.

Enclosed is a Deposit Declaration with an attached copy of the Receipt of an Original Deposit, indicating that hybridoma cell line L106 was deposited at the American Type Culture Collection on November 3, 1993, and given the ATCC designation HB 11483. In light of the filing

of this Deposit Declaration, this rejection under 35 U.S.C. § 112, first paragraph is moot, and withdrawal of this rejection is respectfully requested.

Claims 64, 67 and 70 have also been rejected under 35 U.S.C. § 112, first paragraph, for purportedly not being enabled by the specification as filed. For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

Claims 64, 67 and 70, as amended, recite that the humanized antibody binds to an ACT-4 receptor polypeptide. Humanized antibodies which bind to an ACT-4 receptor polypeptide, as claimed by claims 64, 67 and 70, are enabled by the specification as filed. As noted on pages 12-14 of the specification as filed, ACT-4 receptor polypeptides will typically exhibit substantial amino acid sequence identity with the amino acid sequence of ACT-4-h-1, which is disclosed in Figure 5. Furthermore, ACT-4 receptors likely share some or all of the topological features found in ACT-4-h-1, and all ACT-4 receptors are believed to have extracellular domains. In light of the fact that proteins having the same function in different species have substantial amino acid sequence identity, and similar topological features, it would be within the skill of one in the art to identify ACT-4 receptors from species other than humans. For example, this could be done by preparing probes from the ACT-4-h-1 gene or protein and using these probes in western or southern blot analysis.

Once ACT-4 receptor polypeptides are identified, methods of identifying monoclonal antibodies which bind to the receptor are well known to one of skill in the art. For example, a murine can be immunized with a preparation containing an ACT-4 receptor (or an immunogenic fragment thereof). From these immunized animals, antibody-producing cells are obtained and immortalized and screened for the production of an antibody which binds to ACT-4.

Once antibodies are obtained which bind to ACT-4, humanized antibodies can be produced

by linking the CDR regions of the murine antibodies identified in the previous step to human constant regions by recombinant DNA techniques. *See* Queen *et al.*, *Proc. Natl. Acad. Sci. USA 86*:10029-10033 (1989).

In light of the above, it is believed that the claimed humanized antibodies are enabled by the specification as filed, and withdrawal of this rejection of the claims is believed to be in order.

Claims 64, 67 and 70 have also been rejected under 35 U.S.C. § 112, first paragraph, for purportedly containing subject matter not described in the specification in such a way as to reasonably convey to one of skill in the art that the Applicants had possession of the claimed invention at the time the application was filed. For at least all of the reasons set forth below, Applicants believe that withdrawal of this rejection is in order.

As noted in the MPEP at section 2163, an applicant may show that an invention is complete by disclosure of identifying characteristics, which provide evidence that applicant was in possession of the claimed invention. Such identifying characteristics include binding specificity.

As noted above, claims 64, 67 and 70, as amended, recite humanized antibodies that specifically bind to an ACT-4 receptor polypeptide and comprise three complementarity determining regions which correspond to the complementarity determining regions of an L106 antibody light chain. The humanized antibody of claim 70 also comprises a humanized heavy chain that comprises three complementarity determining regions corresponding to the complementarity determining regions of an L106 antibody heavy chain. Applicants have identified an ACT-4 receptor polypeptide, ACT-4-h-1. Therefore, the antigens to which the humanized antibodies specifically bind have been sufficiently disclosed by the filed specification. Furthermore, Applicants have also disclosed a hybridoma that produces the antibody L106. One of skill in the art

could determine the complementarity determining regions of the L106 antibody light and heavy chains by studying the L106 antibody. The disclosure in the specification as filed of these identifying characteristics of the humanized antibodies is evidence that the Applicants were in possession of the claimed invention at the time the application was filed.

In light of these remarks, Applicants respectfully request withdrawal of each of these rejections under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. 112, Second Paragraph

Claims 31, 60, 64, 65, 67, 68, 70 and 71 have been rejected under 35 U.S.C. § 112, second paragraph, for purportedly being indefinite. According to the Examiner, the claims are indefinite for reciting "L106" antibody, without any identifying characteristics. By the present amendment, the claims have been amended to recite a monoclonal antibody that specifically binds to an ACT-4-h-1 receptor polypeptide and is generated by hybridoma HBL106, deposited under ATCC Accession No. HB 11483, thereby providing identifying characteristics of L106.

In light of these remarks, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. § 102(b)

Claims 31, 59 and 62 have been rejected under 35 U.S.C. § 102(b) for purportedly being anticipated by Knapp *et al.* (Leucocyte Typing IV, 1989). For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

It is well settled that prior art under 35 U.S.C. §102(b) must sufficiently describe the claimed

invention to have placed the public in possession of it. *In re Donahue*, 197 USPQ 1 (C.C.P.A. 1978). In other words, prior art must be enabling. Possession of an invention is clearly not provided if one of ordinary skill in the art could not have combined the publications description of the invention with his own knowledge to arrive at the invention. That is the case here, *i.e.* the reference does not put the skilled artisan in possession of a L106 antibody, and therefore is not enabling. A reference which is not enabling is not an anticipation. *Id.*

Knapp *et al.* does not place the public in possession of the claimed invention. There is no inherent indication that the clone of the cited art possessed the claimed properties (*i.e.* ability to bind to ACT-4-h-1). Knapp *et al.* does not provide guidance regarding what, if any, biological attributes such a clone might have.

Since Knapp *et al.* does not sufficiently describe the claimed invention (*i.e.* antibodies which bind to ACT-4-h-1), Knapp *et al.* has not placed the public in possession of the claimed invention and therefore is not an enabling reference and does not anticipate the claimed invention under 35 U.S.C. §102(b).

Furthermore, there is no way to determine if the antibody designated as L106 (and A6 and A006) is the same as the antibody claimed in the present invention. There is no teaching or suggestion in the Knapp *et al.* reference that the antibody designated A6 (L106) might possess a binding specificity for an antigen other than CD25, such as the ACT-4-h-1 receptor polypeptide of the present invention. In fact, the detailed screening program described in Knapp *et al.*, taken with the fact that Knapp *et al.* demonstrate that the antibody designated A6 (L106) therein is specific for

the CD25 antigen, and only the CD25 antigen, implies that the antibody designated A6 (L106) antibody would not have a binding specificity for an antigenic entity other than CD25.

In light of these remarks, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 102(b).

Rejections Under 35 U.S.C. § 103(a)

Claim 33 has been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over Knapp *et al.* in view of Thorpe *et al.* (*Immunological Rev.* 1982). Claims 35, 60, 61 and 64-72 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over Knapp *et al.* in view of Owens *et al.* (*J. Immunol. Method.*, 1994) and Bird *et al.* (*Science*, 1988). For at least all of the reasons set forth below, withdrawal of these rejections are believed to be in order.

As discussed in more detail above, Knapp *et al.* is not an enabling reference. Since Knapp *et al.* is not an enabling reference, it cannot be combined with other references for a rejection under 35 U.S.C. §103(a).

Moreover, obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Even if the Examiner had established the inherency of the binding of the L106 antibody of Knapp *et al.* to ACT-4-h-1, this characteristic would not be obvious. Therefore, Knapp *et al.* does not disclose or even suggest an L106 antibody which binds to ACT-4-h-1.

In Knapp *et al.*, an antibody, designated L106 (also referred to in Knapp *et al.* as A6 and A006) was employed in an antigen screening program and found to be specific and exclusive for binding to the well known T-cell antigen, CD25. This result is clearly demonstrated throughout the Knapp *et al.* disclosure. For example, the Examiner is directed to page 398, Table 7 of Knapp *et al.*, wherein it is indicated that the A6 (L106) antibody is specifically associated with the CD25 antigen and with no other antigen tested. Additionally, the Examiner is directed to page 487, left column, lines 9-10, of Knapp *et al.* wherein it is stated that the A6 (L106) antibody is specific for the CD25 antigen. Further, it is also stated by Knapp *et al.* that A6 (L106) is specific for the CD25 antigen at page 488, Table 1, and page 496, left column, lines 13-14.

None of the secondary references (*i.e.* Thorpe *et al.*, Owens *et al.* and Bird *et al.*) solve the deficiencies of Knapp *et al.* None of the secondary references disclose or suggest an L106 antibody which specifically binds to ACT-4-h-1. Therefore, even if taken together, the combined disclosures of Knapp *et al.* and Thorpe *et al.*, or Knapp *et al.*, Owens *et al.* and Bird *et al.*, would not disclose or suggest the claimed invention, which is directed to a monoclonal antibody that specifically binds to an ACT-4-h-1 receptor polypeptide (and a fragment thereof, and a humanized antibody which specifically binds to ACT-4-h-1, and an immunotoxin comprising an L106 antibody which binds to ACT-4-h-1).

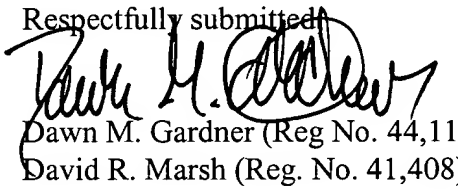
In light of these remarks, Applicants respectfully request withdrawal of these rejections under 35 U.S.C. § 103(a).

Conclusion

In view of the foregoing amendments, Applicants believe the application is in condition for allowance and solicit a Notice of Allowance indicating such at the earliest possible time. Applicants do not believe that any fees are due at this time other than the extensions of time under 37 C.F.R. § 1.136(a). However, if any fees are required, then the Commissioner is authorized to deduct the fees from Arnold & Porter Deposit Account No. 50-2387 referencing matter 16524.010.

The Examiner is encouraged to contact the undersigned should any additional information be necessary.

Respectfully submitted,



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Marked Up Version of Amended Claims Pursuant to 37 C.F.R. 121

35. (Amended) A fragment of a monoclonal [the] antibody [of claim 31] generated by hybridoma HBL106, deposited under ATCC Accession No. HB11483, that specifically binds to an ACT-4-h-1 receptor polypeptide.

60. (Amended) A fragment of an L106 antibody that specifically binds to an ACT-4-h-1 receptor polypeptide with a binding affinity of at least 10^7 M, wherein said L106 antibody is produced by hybridoma HBL106, deposited under ATCC accession No. HB11483.

64. (Amended) A humanized antibody which binds to an ACT-4 receptor polypeptide comprising a humanized heavy chain, wherein the humanized heavy chain comprises three complementarity determining regions corresponding to the complementarity determining regions of an L106 antibody heavy chain, wherein said L106 antibody is produced by hybridoma HBL106, deposited under ATCC accession No. HB11483.

67. (Amended) A humanized antibody which binds to an ACT-4 receptor polypeptide comprising a humanized light chain, wherein the humanized light chain comprises three complementarity determining regions corresponding to the complementarity determining regions of an L106 antibody light chain, wherein said L106 antibody is produced by hybridoma HBL106, deposited under ATCC accession No. HB11483.

70. (Amended) A humanized antibody which binds to an ACT-4 receptor polypeptide

comprising (a) a humanized light chain, wherein the humanized light chain comprises three complementarity determining regions corresponding to the complementarity determining regions of an L106 antibody light chain, and (b) a humanized heavy chain, wherein the humanized heavy chain comprises three complementarity determining regions corresponding tot he complementarity determining regions of an L106 antibody heavy chain, wherein said L106 antibody is produced by hybridoma HBL106, deposited under ATCC accession No. HB11483.